Evaluating the use, performance and acceptability of utility measurement approaches in geographic atrophy, a severe vision disorder

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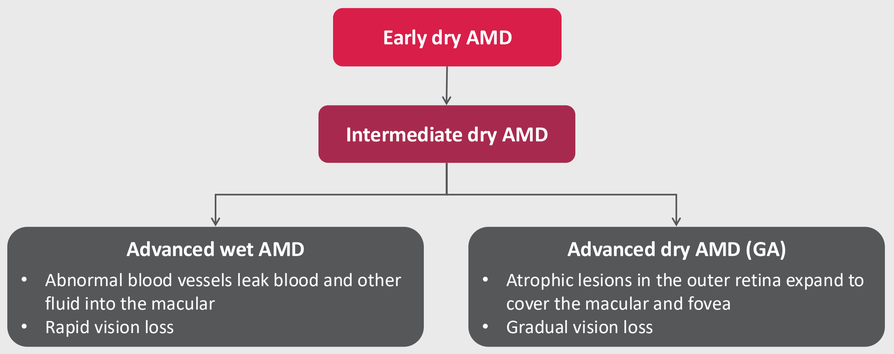
Background

- Age-related macular degeneration (AMD) is a progressive retinal disease that causes central vision loss. The disease has three distinct stages: early, intermediate and advanced AMD.[1]
- Advanced AMD can manifest in two forms, wet AMD and dry AMD. Geographic atrophy (GA) is the advanced form of dry AMD (Figure 1).[1]
- GA interferes with daily activities such as driving, reading, writing and recognising faces which in turn impacts patients' quality of life, mobility, autonomy and independence.[2]
- Measuring the impact of vision loss on health-related quality of life (HRQL) to support cost-effectiveness analyses is challenging. Generic measures like the EQ-5D may be insensitive to the impact of visual impairment.[3]

Figure 1. Overview of the stages and forms of AMD

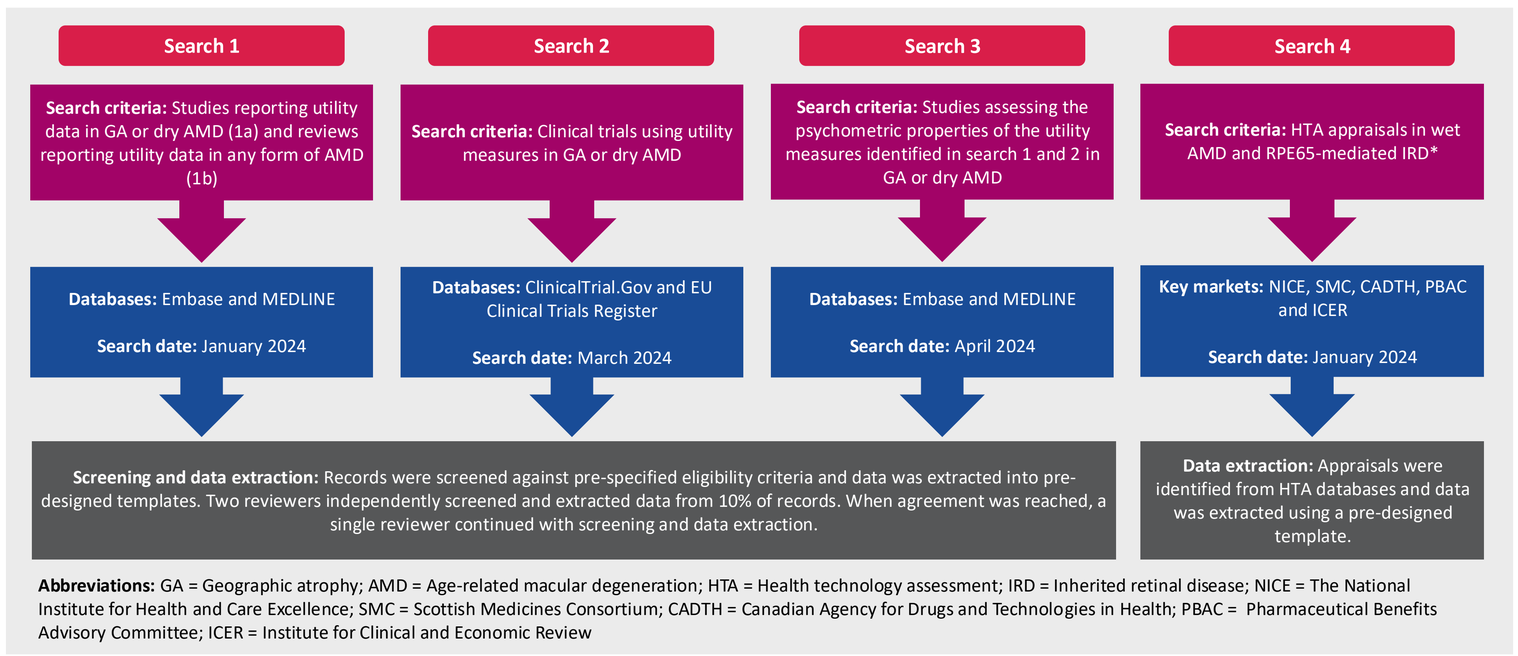


Objective: This review aimed to explore utility (HRQL) measurement approaches in GA and related vision disorders.

Methods

- Four searches were conducted to meet the study objective. Review methods are outlined in Figure 2 (see supplementary materials for full eligibility criteria and search strategies).

Figure 2. Overview of review methods



Abbreviations: GA = Geographic atrophy; AMD = Age-related macular degeneration; HTA = Health technology assessment; IRD = Inherited retinal disease; NICE = The National Institute for Health and Care Excellence; SMC = Scottish Medicines Consortium; CADTH = Canadian Agency for Drugs and Technologies in Health; PBAC = Pharmaceutical Benefits Advisory Committee; ICER = Institute for Clinical and Economic Review

*HTA appraisals in comparable retinal diseases were selected as scoping searches did not identify any appraisals in GA or dry AMD

Results

- PRISMA flow diagrams and summary data extraction tables can be located in the supplementary materials.

Search 1a – Studies reporting utility data in GA or dry AMD

- Three cross-sectional studies were identified which used utility methods or measures in GA populations.[4-6] Two studies used EQ-5D but only one reported utility values. One study used the time trade-off (TTO) method with visually healthy participants who valued different sized simulated scotomas (Table 1).

Table 1. Overview of studies reporting utility data in GA

Author (Date)	Utility method	Sample (N)	Mean utility values (SD)
Enoch et al. (2023)[4]	EQ-5D-5L administered verbally	Individuals with GA (n=30)	EQ-5D index scores not reported*
Crabb et al. (2021)[5]	Four different sized simulated scotomas applied to films of everyday scenes valued using TTO	Individuals with normal vision (n=75)	Very large scotoma: 5.0 (2.7) years of perfect health traded** Very small scotoma: 1.9 (1.4) years of perfect health traded Central scotoma obscuring 5% of film: 2.6 (1.9) years of perfect health traded Central scotoma obscuring 8% of film: 3.5 (2.1) years of perfect health traded
Higgins et al. (2020)[6]* **	EQ-5D (version not reported)	Individuals with no macular disease (n=11), early/intermediate AMD (n=16) and GA (n=22)	No macular disease = 0.81 Early/intermediate AMD = 0.88 GA = 0.82

*Requested from authors; **Values reported as number of years of perfect health traded to avoid 10 years in the health state, rather than 0-1 utility value; ***Identified from review paper identified through the search (Aggarwal et al., 2023).[7]

Search 1b – Reviews reporting utility data in any form of AMD

- Eleven review articles[3, 18-20] were identified in AMD that included studies deriving utilities using TTO, EQ-5D, standard gamble (SG), Health Utilities Index-3 (HUI-3), Short Form 6-Dimension (SF-6D) and Visual Function Questionnaire-25 (VFQ-25) mapped to EQ-5D.
- Only one review article[17] reported utility values by visual acuity (VA) from three studies (Table 2).[18-20] Data were reported by VA in the better-seeing eye (BSE).
  - In the remaining review articles, utilities from the included studies were either not reported or a single value was reported (often without data on the visual function of the measurement population) and so are not included here.

Table 2. Utility values from studies of AMD patients presented by VA in the BSE

Author (Date)	Utility method	Sample (N)	VA in BSE (Snellen)	Mean utility values (SD)
Aspinall et al. (2007)[18]	TTO (valuation of own health)	AMD patients (n=122)	20/20 to 20/25	0.93
			20/30 to 20/40	0.86
			20/50 to 20/100	0.74
			≤20/200	0.68
Brown et al. (2002)[19]	TTO (valuation of own health)	AMD patients (n=246)	20/20 to 20/25	0.84 (0.21)
			20/30 to 20/40	0.80 (0.19)
			20/50 to 20/100	0.71 (0.22)
			≤20/200	0.59 (0.22)
Lee et al. (2008)[20]	SG (valuation of own health)	AMD patients (n=44)	20/20 to 20/25	0.89 (0.23)
			20/30 to 20/40	0.76 (0.30)

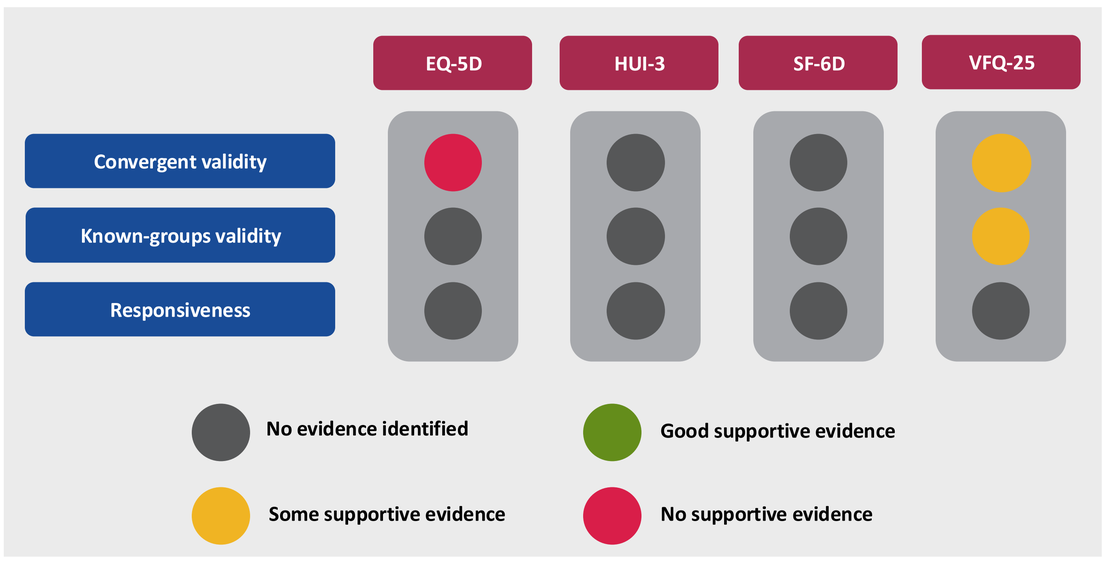
Search 2 – Clinical trials using utility measures in GA or dry AMD

- One ongoing trial was identified in dry AMD which used EQ-5D-5L. Utility values were not reported (EudraCT number: 2017-003899-31).

Search 3 – Psychometric performance of utility measures in GA or dry AMD

- Six studies in GA included evidence of convergent validity and known-groups validity for the VFQ-25 (Figure 3).[21-26]
  - Utilities can be derived from the VFQ-25 using the VFQ-Utilities Index (VFQ-UI).[27,28]
- VFQ-25 scores were significantly associated with structural and functional measures of visual function.[21-26]
- VFQ-25 discriminated between GA vs early/intermediate AMD groups, GA vs non-GA groups and low vs high reading ability groups.[21,22,256,26]
- One study using EQ-5D found no evidence of convergent validity between EQ-5D index scores and performance measures across a series of visual function tasks.[6]
- No psychometric evidence was identified on the performance of the HUI-3 and SF-6D in GA or dry AMD.

Figure 3. Overview of psychometric evidence on the performance of utility measures in GA



Search 4 – HTA appraisals

- Seven appraisals were identified for recommended wet AMD treatments (Table 3). In most appraisals, the utility data was poorly reported and there was limited feedback from the appraisal committee about the utility data.

Table 3. Overview of appraisals for recommended wet AMD treatments

	Utility data submitted by manufacturer	
HTA agency (date) ***Treatment***	**Utility method and population**	**Utility values**
NICE (2008) *Ranibizumab*	TTO (direct elicitation)* – no further details provided	Lowest VA group (<3/60) = 0.497** Highest VA group (≥6/15) = 0.864 Mean difference = 0.367
NICE (2013) *Aflibercept*	EQ-5D with wet AMD patients (n=1240) from VIEW 2 trial[29]	Not reported
SMC (2007) *Ranibizumab*	TTO among members of the general public* – no further details provided	Not reported
SMC (2013) *Aflibercept*	EQ-5D with wet AMD patients (n=1240) from VIEW 2 trial[29]	Not reported
CADTH (2008) *Ranibizumab*	Not reported (based on confidential study sponsored by manufacturer)*	Not reported
CADTH (2019) *Brolucizumab*	EQ-5D* – no further details provided	86 to 100 letters = 0.869*** 71 to 85 letters = 0.772 56 to 70 letters = 0.674 41 to 55 letters 0.577 26 to 40 letters 0.480 0 to 25 letters 0.347
CADTH (2022) *Faricimab*	TTO with healthy participants (n=108) for AMD states simulated using contact lenses[30]	Not reported

*Reference not clear or not provided; **Utilities based on impaired vision in both eyes; ***Utilities classified by BSE

- Four appraisals were identified for RPE65-mediated IRD treatments. In three appraisals, utilities were taken from a study in which vignettes were valued by clinicians using the HUI-3 or EQ-5D.[31]
  - Using clinicians as proxies was criticised by appraisal committees as were the HUI-3 values from the study which were thought to lack face validity.

Conclusion

- This review found limited published utility data and psychometric evidence on the performance of utility measures in GA or dry AMD.
- There is some psychometric evidence to support the use of the VFQ-25 in GA, but more work is needed to explore if this supports the use of the VFQ-UI (utility measure).
- Most evidence suggests generic measures of HRQL such as the EQ-5D are not sensitive to the effect of vision loss on HRQL in AMD.
  - Future work could try to document why this is.
- Existing economic evaluations in wet AMD cited poor quality evidence from research conducted over 15 years ago.
- Very little published data is a significant limitation here.
- We would like HTA bodies to encourage or insist that outcomes data in submissions is published in full.
- **With the emergence of new therapies, new and better methods are needed for accurately measuring the impact of GA on HRQL to support economic evaluation.**

SUMMARY

- This review explored utility (HRQL) measurement approaches in GA and related vision disorders and found limited published utility data and psychometric evidence on the performance of utility measures in GA or dry AMD.
- Some psychometric evidence supports the use of the VFQ-25 in GA, but more research is needed to determine if this supports the use of the VFQ-UI (utility measure). Generic measures like EQ-5D appear to lack sensitivity in capturing the impact of vision loss on HRQL in AMD.
- Existing economic evaluations in wet AMD cited poor quality and outdated evidence.
- With the emergence of new therapies, improved methods are needed to accurately measure the impact of GA on HRQL to support economic evaluation.

ABBREVIATIONS AMD, Age-related macular degeneration; BSE, Better-seeing eye; CADTH, Canadian Agency for Drugs and Technologies in Health; GA, Geographic atrophy; HRQL, Health-related quality of life; HTA, Health technology assessment; HUI-3, Health Utilities Index-3; IRD, Inherited retinal disease; ISPOR, International Society for Pharmacoeconomics and Outcomes Research; NICE, National Institute for Health and Care Excellence; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RPE65, 65-kDA Retinal Pigment Epithelium; SD, Standard deviation; SF-6D, Short Form 6-Dimension; SG, Standard gamble; SMC, Scottish Medicines Consortium; TTO, Time trade-Off; VA, Visual acuity; VFQ-25, Visual Function Questionnaire-25; VFQ-UI, Visual Function Questionnaire-Utilities Index.

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*Full reference list in supplementary materials.

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Supplementary materials